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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,681	01/16/2002	Daniel Cohen	G-101.US05REG	1458

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 09/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/051,681	COHEN ET AL.
	Examiner	Art Unit
	Rebecca E. Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,21,30-32,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,21,30,32,44 and 45* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-19, 22-29, and 33-43 have been canceled. Claims 20, 21, 30-32 and newly presented claims 44-45 are still at issue and are present for examination.

Applicants' arguments filed on 6/13/05, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Prendergast et al. (US PG-PUBS 2004/0053989) in view of Swiss-Prot Accession No. P14920. The rejection is explained in the previous Office Action.

Applicants traverse the rejection by arguing that the rejection is improper as the combination of references fails to teach the limitations recited within the presently claimed invention as Prendergast et al. fail to teach an assay for identifying inhibitors of DAO and thus is devoid of any teaching of the recited method steps and the teachings of the SwissProt polypeptide sequence does nothing to remedy this defect in Prendergast et al. However the recited method steps are the standard means known in the art for assaying for compounds which modulate an enzyme. As evidence of this fact the examiner herein cites Yue et al. (US PGPUBS 2003/0124106) which teaches the exact same steps for assaying for compounds bind and/or modulate a large number of oxidoreductase enzymes (the same class of enzymes which includes the recited DAO protein). See particularly paragraphs 25 and 26 of Yue et al. Hundreds of other patents or literature documents could be used to illustrate that the specific steps of the assay (i.e., assaying enzymatic activity in the presence and absence of the compound and comparing the results) were well known to the skilled artisan at the time of applicants invention as a method of determining if a test compound inhibits an enzyme of interest. As such the teachings of Prendergast et al. and Swiss-Prot Accession No. P14920 which clearly provides motivation for

assaying for inhibitors of the DAO of SEQ ID NO:7 clearly makes obvious the instantly claimed methods as a skilled artisan would have found it obvious to use the known formats of inhibitor screening assays to do so.

Applicants further argue that the rejection is also the result of improper hindsight reconstruction of the claimed invention. Applicants argue that applicant's disclosure has been used to serve as the basis of the rejection currently of record because there is no motivation for one of ordinary skill in the art to apply the cited teachings without the guidance and disclosure of the presently claimed invention. This is not persuasive because Prendergast et al. without a doubt provides motivation for the instantly claimed methods. Pendergast et al. teach that DAO inhibitors are useful for treatment of Alzheimers and other diseases which clearly are substantial health problems in the world. As such a skilled artisan would clearly desire to obtain a variety of such compounds in order to have a large selection of compounds to use to address these diseases and would be motivated to test a variety of molecules to determine if they have this capability.

Claims 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prendergast et al. (US PG-PUBS 2004/0053989) in view of Swiss-Prot Accession No. P14920 as

applied to claim 21 above, and further in view of Ricci et al. (Reference R43 of applicants IDS of 12/30/02).

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Claims 20, 21, 44 and 451 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsai et al (US PG-PUBS 2002/0035145) in view of Wake et al. and Swiss-Prot Accession No. P14920.

Applicants repeat the arguments presented in traverse of the rejection of Claim 21 over Prendergast et al. (US PG-PUBS 2004/0053989) in view of Swiss-Prot Accession No. P14920 with regard to the lack of teaching of the specific method steps of the instant claims within the cited references. However, as explained above the recited steps are standard in the art for screening for inhibitors of an enzyme of interest. Since the cited reference provide motivation for screening for inhibitors of the DAO of SEQ ID NO:7, the instant claimed methods are obvious to one of skill in the art.

Applicants argue that the combination of references do not render the claimed inventions obvious as there is no teaching or suggestion that increased or abnormal human DAO activity is

associated with the schizophrenia, depression, or bipolar disorder nor is there any teaching in the cited combination of references that decreased levels of D-serine are associated with schizophrenia, depression, or bipolar disorder. This is not persuasive because Tsai et al. et al. explicitly teach that neuropsychiatric disorders including schizophrenia and depression can be treated using agonists of the glycine site of the NDMA receptor including D-serine which Wake et al. teach is the endogenous agonist of the glycine site of the NDMA receptor. Furthermore, Wake et al. teach that the endogenous enzyme D-amino acid oxidase degrades D-serine and that therefore DAO may exert modulatory action on NDMA receptor activity by controlling the concentration of D-serine. As such a skilled artisan would reasonably expect inhibitors of D-serine degradation to be useful for increasing the endogenous concentration of D-serine and therefore to be similarly useful for the treatment of schizophrenia and depression.

Claims 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsai et al (US PG-PUBS 2002/0035145) in view of Wake et al. and Swiss-Prot Accession No. P14920 as applied to claim 20, 21, 44 and 45 above, and further in view of Ricci et al. (Reference R43 of applicants IDS of 12/30/02).

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Claims 20, 21, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsai et al (US PG-PUBS 2002/0035145) in view of Snyder et al. (Reference R47 of applicants IDS of 12/30/02), and Swiss-Prot Accession No. P14920.

Applicants repeat the arguments presented in traverse of the rejection of Claim 21 over Prendergast et al. (US PG-PUBS 2004/0053989) in view of Swiss-Prot Accession No. P14920 with regard to the lack of teaching of the specific method steps of the instant claims within the cited references. However, as explained above the recited steps are standard in the art for screening for inhibitors of an enzyme of interest. Since the cited reference provide motivation for screening for inhibitors of the DAO of SEQ ID NO:7, the instant claimed methods are obvious to one of skill in the art.

Applicants argue that the combination of references do not render the claimed inventions obvious as there is no teaching or suggestion that increased or abnormal human DAO activity is associated with the schizophrenia, depression, or bipolar

disorder nor is there any teaching in the cited combination of references that decreased levels of D-serine are associated with schizophrenia, depression, or bipolar disorder. This is not persuasive because Tsai et al. et al. explicitly teach that neuropsychiatric disorders including schizophrenia and depression can be treated using agonists of the glycine site of the NDMA receptor including D-serine which Synder et al. teach is the endogenous agonist of the glycine site of the NDMA receptor. Furthermore, Synder et al. teach that the endogenous enzyme D-amino acid oxidase degrades D-serine and show that exogenously applied DAO inhibits NDMA neurotransmission (see page 557) and that this inhibition can be fully reversed by D-serine application. As such a skilled artisan would reasonably expect inhibitors of D-serine degradation to be useful for increasing the endogenous concentration of D-serine and therefore to be similarly useful for the treatment of schizophrenia and depression.

Claims 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsai et al (US PG-PUBS 2002/0035145) in view of Snyder et al. (Reference R47 of applicants IDS of 12/30/02) and Swiss-Prot Accession No. P14920 as applied to claim 20, 21, 44 and 45 above, and further in view of Ricci et al. (Reference R43 of applicants IDS of 12/30/02).

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Claim 31 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The examiner cannot find any teaching in the prior art that the compounds cystathionine ketimine and cyclothionine were known to be D-amino acid oxidase inhibitors. As such there would have been no motivation for a skilled artisan to select these particular compounds as test compounds in a screen for DAO inhibitors.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rebecca Prouty
Primary Examiner
Art Unit 1652